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**PATENT APPLICATION**  
**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

First Applicant: Mark Louis Heiman

For: USES OF MELANOCORTIN-4 RECEPTOR (MC4R) AGONIST  
PEPTIDES ADMINISTERED BY CONTINUOUS INFUSION

Docket No.: X-16438

**INFORMATION DISCLOSURE STATEMENT**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

As a means of complying with the duty of disclosure, Applicants submit an "Information Disclosure Citation in an Application" on a Form PTO-1449 (modified) and provide a copy of each of the listed documents for consideration by the Examiner.

Since this Statement is being filed in accordance with 37 C.F.R. 1.97(b), Applicants submit that no additional fee is required.

Applicants request consideration of this information.

Respectfully submitted,

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Attorney for Applicants  
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4 August 2006

AUG 6 2008

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Sheet 1 of 6

FORM PTO 1449 (modified)  INFORMATION DISCLOSURE CITATION IN AN APPLICATION		Atty. Docket No. X-16438	Serial No. <b>10/588667</b>
		First Applicant Mark Louis Heiman	
		Filing Date	Group

**U.S. PATENT DOCUMENTS**

Examiner Initials*	Cite No. 1	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines. Where Relevant Pages or Relevant Figures Appear
		Number-Kind Code <sup>2</sup> (if known)			
	AA	US 5,674,839	10-07-1997	Hruby, et al.	
	AB	US 6,579,968	06-17-2003	Blood, et al.	
	AC	US 6,659,982	12-09-2003	Douglas, et al.	
	AD	US 6,716,810	04-06-2004	Brennan, et al.	
	AE	US 6,794,489	09-21-2004	Blood, et al.	
	AF	US 2002/143141	10-03-2002	Yagaloff et al.	
	AG	US 2002/0107182	08-08-2002	Blood, et al.	
	AH	US 2005/0037951	02-17-2005	Blood, et al.	

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. 1	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines. Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Country Code <sup>3</sup> -Number <sup>4</sup> - Kind Code <sup>5</sup> (if known)				
	BA	EP 0 292 291	08-10-1994	Hruby et al.		
	BB	EP 1 196 184	04-20-2005	Blood et al.		
	BC	WO 98/37097	08-27-1998	Wikberg et al		

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	BD	WO 99/54358	10-28-1999	Adan et al.		
	BE	WO 00/33658	06-15-2000	Brennan et al.		
	BF	WO 00/35952	06-22-2000	Wikberg et al.		
	BG	WO 00/58361	10-05-2000	Mazur et al.		
	BH	WO 01/00224	01-04-2001	Blood et al.		
	BI	WO 02/18437	03-07-2002	Chen et al.		
	BJ	WO 03/006604	01-23-2003	Bednarek		
	BK	WO 03/072072	09-04-2003	Dorr et al.		

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(AP20 Rec'd 8/1/04 04 AUG 2006)

FORM PTO 1449 (modified)		Atty. Docket No. X-16438	Serial No.
INFORMATION DISCLOSURE CITATION IN AN APPLICATION		First Applicant Mark Louis Heiman	
		Filing Date	Group

## NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. 1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s) publisher, city and/or country where published.	T <sup>6</sup>
	CA	BALSE-SRINIVASAN, P. et al. "Structure-Activity Relationships of $\gamma$ -MSH Analogues at the Human Melanocortin MC3, MC4, and MC5 Receptors. Discovery of Highly Selective hMC3R, hMC4R, and hMC5R Analogues." <i>J. Med. Chem.</i> , Vol. 46, pp. 4965-4973, 2003.	
	CB	BALSE-SRINIVASAN, P. et al. "Structure-Activity Relationships of Novel Cyclic $\alpha$ -MSH/ $\beta$ -MSH Hybrid Analogues That Lead to Potent and Selective Ligands for the Human MC3R and Human MC5R." <i>J. Med. Chem.</i> , Vol. 46, pp. 3728-3733, 2003.	
	CC	BERNATOWICZ, M. et al. "1H-Pyrazole-1carboxamidine Hydrochloride: An Attractive Reagent for Guanylation of Amines and Its Application to Peptide Synthesis." <i>J. Org. Chem.</i> , Vol. 57, pp.2497-2502, 1992.	
	CD	BUTLER, A. et al. "A Unique Metabolic Syndrome Causes Obesity in the Melanocortin-3 Receptor-Deficient Mouse." <i>Endocrinology</i> , Vol. 141, No.9, pp. 3518-3521, 2000.	
	CE	CHE, A. et al. "Inactivation of the Mouse Melanocortin-3 Receptor Results in Increased Fat Mass and Reduced Lean Body Mass." <i>Nature Genetics</i> , Vol. 26, pp. 97-102, 2000.	
	CF	CHEUNG, A. et al. "Structure-Activity Relationship of Linear Peptide Bu-His-DPhe-Arg-Trp-Gly-NH <sub>2</sub> at the Human Melanocortin-1 and -4 Receptors: Histidine Substitution." XP001183563, <i>Bioorganic and Medicinal Chemistry Letters</i> , Vol. 13, pp. 133-137, 2003.	
	CG	CHHAJLANI, V. "Distribution of cDNA For Melanocortin Receptor Subtypes In Human Tissues." <i>Biochemistry and Molecular Biology International</i> , Vol. 38, pp. 73-80, 1996.	
	CH	FAN, W. et al. "The Central Melanocortin System Can Directly Regulate Serum Insulin Levels." <i>Endocrinology</i> , Vol. 141, No. 9, pp. 3072-3079, 2000.	
	CI	GANTZ, I. et al. "Molecular Cloning of a Novel Melanocortin Receptor." <i>The Journal of Biological Chemistry</i> , Vol. 268, No. 11, pp. 8246-8250, 1993.	
	CJ	GARCIA-ECHEVERRIA, et al. "Conformational Analysis of Two Cyclic Disulfide Peptides." <i>Biopolymers</i> , Vol. 31, pp. 835-843, 1991.	
	CK	HAN, G. et al. "De Novo Design, Synthesis, and Pharmacology of $\alpha$ -Melanocyte Stimulating Hormone Analogues Derived from Somatostatin by a Hybrid Approach." <i>J. Med. Chem.</i> , Vol. 47, pp. 1514-1526, 2004.	

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FORM PTO 1449 (modified)  INFORMATION DISCLOSURE CITATION IN AN APPLICATION			Atty. Docket No. X-16438	Serial No. 112383607
			First Applicant Mark Louis Heiman	
			Filing Date	Group
	CL	HASSELL-LUEVANO, C. et al. "Characterization of Melanocortin NDP-MSH Agonist Peptide Fragments at the Mouse Central and Peripheral Melanocortin Receptors." XP-002970859. J. Med. Chem. Vol. 44, pp. 2247-2252, 2001.		
	CM	HOLDER, J. and HASSELL-LUEVANO, C. "Melanocortin Ligands: 30 Years of Structure-Activity Relationship (SAR) Studies." Medicinal Research Reviews, Vol. 24, No. 3, pp. 325-356, 2004.		
	CN	HOLDER, J. et al. "Structure-Activity Relationships of the Melanocortin Tetrapeptide Ac-His-DPhe-Arg-Trp-NH <sub>2</sub> at the Mouse Melanocortin Receptors. 1. Modifications at the His Position." J. Med. Chem., Vol. 45, pp. 2801-2810, 2002.		
	CO	HRUBY, V. et al. "Design of Novel Melanotropin Antagonists for the Recently Discovered MC3, MC4 and MC5 Receptors and Their Use to Determine New Biological Roles." Peptides: Frontiers of Peptide Science, Proc Am. Pept. Symp. 15 <sup>th</sup> , pp. 723-725, 1997.		
	CP	HRUBY, V. et al. "Design and Bioactivities of Melanotropic Peptide Agonists and Antagonists: Design Based on a Conformationally Constrained Somatostatin Template." Letters in Peptide Science, Vol. 5, pp. 117-120, 1998.		
	CQ	HRUBY, V. et al. "Conformational Considerations in the Design of Highly Potent and Long-Acting Peptide Hormone Agonists and Antagonists." Peptides: Proc Eur Pept Symp 17 <sup>th</sup> , pp. 19-30, 1982.		
	CR	HRUBY, V. et al. "Synthesis of a Cyclic Melanotropic Peptide Exhibiting Both Melanin-Concentrating and -Dispersing Activities." Science, Vol. 224, pp. 1111-13, 1984.		
	CS	HSIUNG, H. et al. "Potent Peptide Agonists for Human Melanocortin 3 and 4 Receptors Derived From Enzymatic Cleavages of Human $\beta$ -MSH (5-22) by Dipeptidyl Peptidase I and Dipeptidyl Peptidase IV." Peptides, Vol. 26, pp. 1988-1996, 2005.		
	CT	HSIUNG, H. et al. "A Novel and Selective Beta-MSH Derived Peptide Agonist For Melanocortin 4 Receptor Potently Decreased Food Intake and Body Weight Gain In Diet-Induced Obese Rats." Endocrinology, pp. 1-39, 2005.		
	CU	KASK, A. et al. "Discovery of a Novel Superpotent and Selective Melanocortin-4 Receptor Antagonist (HS024): Evaluation <i>in Vitro</i> and <i>in Vivo</i> ." Endocrinology, Vol. 139, No. 12, pp. 5006-5014, 1998.		
	CV	KIM, M. et al. "The Central Melanocortin System Affects the Hypothalamopituitary Thyroid Axis and May Mediate the Effect of Leptin." The Journal of Clinical Investigation, Vol. 105, No. 7, pp. 1005-1011. 2000.		

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		First Applicant Mark Louis Heiman	
		Filing Date	Group
	CW	KIM, M. et al. "Hypothalamic Localization of the Feeding Effect of Agouti-Related Peptide and $\alpha$ -Melanocyte-Stimulating Hormone." <i>Diabetes</i> , Vol. 49, pp. 177-182, 2000.	
	CX	KUCZMARSKI, R. "Prevalence of Overweight and Weight Gain in the United States." <i>Am. J. Clin. Nutr.</i> Vol. 55, pp. 495S-502S, 1992.	
	CY	LICHA, K. et al. "Synthesis, Characterization, and Biological Properties of Cyanine-Labeled Somatostatin Analogues as Receptor-Targeted Fluorescent Probes." <i>Bioconjugate Chem.</i> , Vol. 12, pp. 44-50, 2001.	
	CZ	MACNEIL, D. et al. "The Role of Melanocortins in Body Weight Regulation: Opportunities for the Treatment of Obesity." <i>European Journal of Pharmacology</i> , Vol. 440, pp. 141-157, 2002.	
	CAB	MARKS, D. and CONE, R. "The Role of the Melanocortin-3 Receptor in Cachexia." <i>Annals of the New York Academy of Sciences</i> , Vol. 994, pp. 258-266, 2003.	
	CAC	MAYER, J. et al. "Discovery of a $\beta$ -MSH-Derived MC-4R Selective Agonist." <i>Journal of Medicinal Chemistry</i> , Vol. 48, No. 9, pp. 3095-3098, 2005.	
	CAD	NASH, I. et al. "Dde – A Selective Primary Amine Protecting Group: A Facile Solid Phase Synthetic Approach to Polyamine Conjugates." <i>Tetrahedron Letters</i> , Vol. 37, No. 15, pp. 2625-2628, 1996.	
	CAE	NI, X. "Genetic Disruption of $\gamma$ -Melanocyte-stimulating Hormone Signaling Leads to Salt-Sensitive Hypertension in the Mouse." <i>The Journal of Clinical Investigation</i> , Vol. 111, No. 8, pp. 1251-1258, 2003.	
	CAF	OBICI, S. et al. "Central Melanocortin Receptors Regulate Insulin Action." <i>The Journal of Clinical Investigation</i> , Vol. 108, No. 7, pp. 1079-1085, 2001.	
	CAG	PROIETTO, J. et al. "Novel Anti-Obesity Drugs." <i>XP-001004696. Exp. Opin. Invest. Drugs</i> , Vol. 9, No. 6, pp. 1317-1326, 2000.	
	CAH	REUDELHUBER, T. "Salt-Sensitive Hypertension: If Only It Were As Simple As Rocket Science." <i>J. Clin. Invest.</i> , Vol. 111, pp. 1115-1116, 2003.	
	CAI	ROSELLI-REHFUSS, L. et al. "Identification of a Receptor for $\gamma$ Melanotropin and Other Proopiomelanocortin Peptides in the Hypothalamus and Limbic System." <i>Proc. Natl. Acad. Sci.</i> , Vol. 90, pp. 8856-8860, 1993.	
	CAJ	SAWYER, T. et al. "[half-Cys <sup>4</sup> , half-Cys <sup>10</sup> ] – $\alpha$ -Melanocyte-stimulating Hormone: A Cyclic $\alpha$ -Melanotropin Exhibiting Superagonist Biological Activity. <i>Proc. Natl. Acad. Sci.</i> , Vol. 79, pp. 1751-1755, March 1982.	
	CAK	SCHAAPER, W. "Synthesis of Cyclic $\alpha$ -MSH Peptides." <i>Letters in Peptide Science</i> , Vol. 5, pp. 205-208, 1998.	

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## NON PATENT LITERATURE DOCUMENTS

CAL	SCHIOTH, H. et al. "Major Pharmacological Distinction of the ACTH Receptor From Other Melanocortin Receptors." Life Sciences, Vol. 59, No. 10, pp. 797-801, 1996.	
CAM	SCHIOTH, H. et al. "Novel Selective Melanocortin 4 Receptor Antagonist Induces Food Intake After Peripheral Administration." Biochemical and Biophysical Research Communications, Vol. 301, pp. 399-405, 2003.	
CAN	SHEARMAN, L. et al. "Chronic MCH-1 Receptor Modulation Alters Appetite, Body Weight and Adiposity in Rats." European Journal of Pharmacology, Vol. 475, pp. 37-47, 2003.	
CAO	VERSTEEG, D. et al. "Melanocortins and Cardiovascular Regulation." European Journal of Pharmacology, Vol. 360, pp. 1-14, 1998.	
CAP	WANG, et al. "p-Alkoxybenzyl Alcohol Resin and p-Alkoxybenzylloxycarbonyl-hydrazide Resin for Solid Phase Synthesis of Protected Peptide Fragments." Journal of Am. Chem. Soc., Vol. 95, pp. 1328-33, 1972.	
CAQ	WESSELLS, H. et al. "Synthetic Melanotropic Peptide Initiates Erections in Men With Psychogenic Erectile Dysfunction: Double-Blind, Placebo Controlled Crossover Study." The Journal of Urology, Vol. 160, No. 2, pp. 389-393, 1998.	
CAR	YAN, L. and Mayer, J. "Use of Trichloroacetimidate Linker in Solid-Phase Peptide Synthesis." Journal of Org. Chem., Vol. 68, pp. 1161-1162, 2003.	
CAS	YAN, L. et al. "Potent and Selective MC-4 Receptor Agonists Based on a Novel Disulfide Scaffold." Bioorganic and Medicinal Chemistry Letters 15, pp. 4611-14, 2005	

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